SYMPTOMATIC ARTHRITIS DUE TO HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY IN PULMONARY NEOPLASTIC DISEASE*

A REPORT OF SEVEN CASES

BY

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Clubbed fingers and hypertrophic osteo-arthropathy have been associated with a wide variety of diseases, including suppurative processes in the chest (Whiteside, 1914; Springthorpe, 1895), chronic gastro-intestinal disorders—such as ulcerative colitis, regional enteritis and sprue, and cirrhosis of the liver—(Schlicke and Bargen, 1940), congenital heart disease (White and Sprague, 1929), subacute bacterial endocarditis (Cotton, 1922), and pulmonary neoplasms (Strangeways and Ponder, 1908). Clubbing of the fingers is not infrequently the first clinical manifestation of pulmonary malignancy, but a polyarthritis due to hypertrophic pulmonary osteo-arthropathy is rarely considered as a possible presenting symptom of a pulmonary tumour (Craig, 1937). During a period of five years we have seen seven patients who presented themselves complaining of "joint pain", "joint swelling", or "arthritis", although the underlying disease was pulmonary malignancy. Three of these patients had been treated for arthritis and the chest lesion had not been recognized for a period of months after treatment for arthritis had been started. In five of the patients joint pain had preceded clubbing—at least to the patient's knowledge. In the absence of radiographs showing subperiosteal bone proliferation, the diagnosis could not have been made in these patients. Because of this, it was felt that a detailed report of these patients would be worth while in order to note certain features of the syndrome and to emphasize that hypertrophic pulmonary osteo-arthropathy must be considered in the investigation of the patient with arthritic complaints.

Case Reports

Case 1.—V.L., a Puerto Rican male, aged 48, was admitted to hospital on August 30, 1948, complaining of pain in his ankles for nine months, pains in his wrists and elbows for three months, and clubbing of the fingers for six weeks. A review of his past medical history was essentially negative except for primary syphilis in 1926 and a weight loss of 20 lb. in eight months. Nine months before admission, he had noticed pain on motion of the left ankle which was worse in inclement weather. His local physician treated him for arthritis but within six weeks he developed similar symptoms in the left knee and subsequently noticed involvement of the elbows, wrists, and hips. Six weeks before

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admission he began to notice clubbing of his fingers. A chest *x* ray taken at another hospital ten months before admission was reported negative.

Physical examination revealed clubbing of the fingers and toes, enlargement of all the joints in the lower extremities, and fluid in the right knee. Laboratory examinations (including complete blood counts, sedimentation rate, and alkaline phosphatase) were within normal limits. *X* rays of the extremities showed marked subperiosteal bone proliferation along the shafts of all the long bones. An *x* ray of the chest showed an ovoid shadow in the right lower lobe of his lung which was thought to be a bronchogenic carcinoma of the right lower lobe. A pneumonectomy was performed on September 9, 1948, and carcinoma of the right lower lobe with metastases to the hilar and pleural nodes was found at operation and proven histologically. He had an uneventful post-operative course. Relief of joint symptoms was noted within several hours following operation. On October 22, 1948, he was seen in the Out-patient Department and had no complaints. There was no objective evidence of arthritis clinically. At this time the right femur and right knee showed no change in the radiographical appearance from the pre-operative films. On June 27, 1949, his only complaint was dyspnoea on exertion and pain in the right chest wall. He was gaining weight rapidly and had no joint symptoms.

Case 2.—N.P.B., a 41-year-old linotype operator, presented himself complaining of " swollen fingers and feet " of eleven weeks' duration. He had also noted a loss of 14 lb. in weight during the same period. He smoked an average of thirty cigarettes daily and had had an excessive alcoholic intake for many years. Past medical history revealed a chronic discharge from his ears for years, as well as a marked post-nasal drip and cough productive of a tablespoonful of sputum every morning for twelve years. On May 22, 1947, the patient noted swelling of both ankles. His physician stated that this was due to " poor circulation " and prescribed vitamins. Two weeks later he began to have sharp pains in both knees and these persisted until his admission to hospital on September 9, 1947. Swelling of his feet had been present for four weeks and redness of his fingertips for three weeks.

Physical examination disclosed a lenticular opacity in the right eye and a watery discharge from both ears. Examination of the chest and abdomen was normal except for hepatomegaly. There was pitting oedema of the ankles and a fusiform swelling of the proximal interphalangeal joints of the fingers, as well as clubbing. The laboratory examinations (including complete blood count, urine analysis, Kline, alkaline phosphatase, and electrocardiogram) were normal except for the sedimentation rate which was 98 mm. in 1 hour. *X* ray of the chest showed a spherical shadow of increased density 2½ cm. in diameter in the lower lateral portion of the right upper lobe of the lung, which was thought to have the appearance of bronchogenic carcinoma. Skeletal survey was negative except for slight thickening of the posterior margin of the cortex of the left fibula in its distal third due to subperiosteal bone production. Pulmonary studies showed minor impairment of pulmonary function.

On October 15, 1947, a right upper lobectomy was performed and bronchogenic carcinoma was found which was confirmed histologically. Three days later there was a definite remission of the arthritic symptoms. His post-operative course was complicated by the development of partial atelectasis of the right lower lobe and pneumonia of that lobe. He was discharged on the thirteenth post-operative day and *x* rays showed complete expansion of the remaining lobes of the right lung. When seen one month later he had no respiratory or joint symptoms and has remained asymptomatic until the present time. *X*-ray examination of the extremities on July 22, 1949, showed no change in the appearance of the subperiosteal bone proliferation.

Case 3.—L.F.B., a 62-year-old shiploader, was admitted to the hospital on February 2, 1949, complaining of joint pains for one year, cough and progressive shortness of breath for eight months. He had smoked forty cigarettes daily for 35 years and had noted a

weight loss of 45 lb. in nine months. His past medical history was otherwise negative except for varicose veins and varicose ulcers several years previously. Twelve months before admission the patient had noted moderately severe pain in his hands and knees. On the advice of his physician he had had all his teeth extracted without relief of his pain. Shortly afterward he developed pleuritic pain in the left lateral chest wall which had persisted continuously up to admission. At the same time he developed a cough with blood-flecked sputum. He had also noticed swelling and tenderness of both nipples for six months, and he had had an audible wheeze for one month and hoarseness for one week. Clubbing of the fingers had been present for eleven months but his physician had told him to " forget it ".

Physical examination revealed paralysis of the left vocal cord, dullness over the left upper chest anteriorly and posteriorly with decreased expansion in this area. The heart showed auricular fibrillation but was not enlarged or otherwise remarkable. The liver was markedly enlarged and varicosities of the left leg were noted. The laboratory examinations (including a complete blood count, urine analysis, cephalin flocculation, alkaline phosphatase, and serum protein partition) were normal. However, the electrocardiogram showed auricular fibrillation and low voltage. The bromosulphalein test showed 20 per cent. retention after 30 minutes. *X* rays of the lungs showed a malignant lesion in the left upper lobe, extending into the overlying ribs. Skeletal survey revealed osteo-arthropathy of the distal ends of the clavicles, both tibiae and fibulae, the metacarpals, and the metatarsals.

Radiotherapy was instituted without relief of any of the chest symptoms or the joint pains and the patient died on June 1, 1949. Permission for an autopsy was not granted.

Case 4.—S.P., a 54-year-old white male, Yugoslav-born, asbestos insulator, was admitted on January 24, 1949, because of clubbing of the fingers of three months' duration. He had noted a weight loss of 20 lb. in the preceding six months. He smoked forty cigarettes daily. Two years previously his left elbow had been aspirated for bursitis. For six months he had had pain in his hips and knees. The other joints became painful gradually and by the time of admission, all the joints of his extremities were involved. Ankle oedema had been present for five months. His presenting symptom of bulbous swellings of the tips of his fingers had been increasing for three months. Three days prior to admission, he began to cough and had expectorated some blood. On physical examination persistent râles were present at the left base, as well as marked clubbing of the fingers and toes, and swelling of the wrists and ankles but there was no pain or redness.

Laboratory examination showed a marked reduction of vital capacity (1,700 ml.) and *x* rays of the lungs demonstrated a slight prominence of the left hilar area. A skeletal *x*-ray survey showed osteo-arthritis of the spine and subperiosteal new bone formation of both femora and tibiae. Bronchoscopy demonstrated bleeding from the left lower lobe bronchus. On exploration, the patient was found to have numerous pleural metastases due to carcinoma from an unknown site. Post-operative palliative radiation was begun but the joint pain had persisted. When last seen on June 6, 1949, he was having severe pain in his chest and the joints of his left arm.

Case 5.—J.P., a 40-year-old Italian fur-dresser, was admitted to the Presbyterian Hospital on July 30, 1944, complaining of swelling of his toes and fingertips and pain in his knees for four months. He smoked one package of cigarettes daily and had noted a productive cough for three years. His past medical history was otherwise negative. Physical examination revealed clubbing of the fingers and toes. His knees were swollen and tender with some joint effusion. Laboratory examinations (including complete blood count, Kline, serum protein partition, calcium, phosphatase, and cephalin flocculation) were within normal limits. Erythrocyte sedimentation rate was 95 mm. in 1 hour. Arterial oxygen saturation was 95 per cent. Catheterization of the right auricle showed only 43 per cent. oxygen saturation of mixed venous blood. *X* rays of the long bones

showed a marked periosteal reaction around the ankles and knees and metatarsals of the feet. Bronchograms were normal and *x* rays of the chest showed prominent markings in the left hilum.

The patient's temperature ranged between 100° and 102° F. and in the eighth week he developed an area of increased density projecting from the left hilum. When thoracotomy was suggested, the patient signed out of the hospital but he returned one month later. *X* rays showed extensive, progressive increase in the size of the mass in the left hilar area. Radiotherapy was attempted but was not well tolerated, and there was no improvement in joint symptoms. The patient was taken home where he died on January 1, 1945.

Case 6.—G.Z.B., a 45-year-old male, was admitted on October 26, 1948, for pain and swelling of the hands, knees, and feet of ten months' duration. His past medical history was non-contributory. Three months previous to admission he had noticed swelling of the ankles and two months previously gradual enlargement of the hands and wrists had begun. For three weeks before admission, he had had a productive cough without haemoptysis. Examination of the chest was normal except for an expiratory wheeze over the right upper lobe. The hands were markedly thickened and there was clubbing of the fingers. There were joint effusions in both knees. The feet were enlarged and swollen with pitting oedema which extended up to the knees.

Laboratory examinations were normal except for elevation of the erythrocyte sedimentation rate to 49 mm. in one hour. *X* rays of the chest revealed a shadow of increased density in the right upper lobe suggestive of bronchogenic carcinoma. Skeletal films showed subperiosteal new bone formation of the ulna, radius, metacarpals, femur, and tibia bi-laterally. On October 28, 1948, a right pneumonectomy was performed and an irregularly firm tumour of the apical portion of the right upper lobe and a nodule in the lower lobe were found which were proven histologically to be bronchogenic carcinoma. There was no lymph-node enlargement. On the first post-operative day the pains in his joints had completely disappeared, although they recurred to a mild degree on the fifth post-operative day. Two months later, he developed low back pain with sciatica, and was found to have pelvic and lumbosacral metastases. Arrangements were made for terminal care.

Case 7.—A.O., a 32-year-old female, entered the Vanderbilt Clinic on June 7, 1949, because of pain in the knees, swelling of the left ankle, and clubbing of the fingers for six months. The patient had had a "giant cell tumour" removed from the extensor tendon of the middle finger of the right hand in March, 1947, at another hospital. In October, 1947, a tumour of similar histopathology was removed from the right wrist. The tumour recurred and the arm was amputated (mid-humerus) in January, 1948. Nodules subsequently appeared in the occipital region of the scalp and the right upper lobe of the lung. Biopsies of the available lesions showed them to be similar in histological appearance but impossible to classify.

In August, 1948, the patient began to have pain and stiffness in both knees with swelling of the left foot and ankle. Subperiosteal bone proliferation of the long bones, metatarsals, and right clavicle was demonstrable by *x* ray, as well as clubbing of the fingers and toes.

Radiotherapy to the subcutaneous nodules, mediastinum, and left ankle caused some clearing. However, the pain in the joints of the extremities had remained severe up to the time she was last seen on July 5, 1949.

Discussion

The patients reported reveal the fact that a pulmonary malignancy, whether primary or secondary, small in size or extensive, may produce the phenomenon of hypertrophic pulmonary osteo-arthropathy. This may result in symptoms and

signs of a severe polyarthritis. Surgical excision of the pulmonary neoplasm was followed by rapid subsidence of joint symptoms in three patients in the present series, although there was no change in the radiographical appearance of the involved bones twenty months after the surgical excision in one patient. When surgical resection of the pulmonary neoplasm was not performed there was no improvement in joint symptoms despite radiation therapy.

Mendlowitz (1942) has suggested that the increase of digital blood flow and the decrease in the brachial-digital arterial pressure gradient which he found to be present in simple non-hereditary clubbing might be related to the pathogenesis of this condition. When body changes and hypertrophic pulmonary osteo-arthropathy were present, the pressure gradient was normal. Mendlowitz proposed that the bone changes were in the nature of a compensatory mechanism. With this exception there is no satisfactory explanation for the finding of clubbed fingers and of hypertrophic pulmonary osteo-arthropathy, particularly that seen associated with small intrapulmonary tumours. In such instances, one might presuppose the elaboration of some osteoblast-stimulating substance by the tumour since there are no abnormalities in pulmonary or cardiac function.

Summary

Seven patients are reported in whom pulmonary osteo-arthropathy was associated with pulmonary neoplasia. In five of these patients joint pains appeared to precede the clubbing of the fingers. In three instances treatment for arthritis had preceded by several months the recognition of the underlying pulmonary lesion. Surgical removal of the tumour relieved the joint symptoms, but did not cause regression of the periosteal lesions.

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Arthrite Symptomatique due à l'Ostéo-arthropathie Pulmonaire Hypertrophique dans la Maladie Pulmonaire Néoplasique

RÉSUMÉ

On relate le cas de sept malades chez qui l'ostéo-arthropathie se trouvait associée à la néoplasie pulmonaire. Chez cinq d'entre eux les douleurs articulaires semblèrent se présenter avant l'apparition des doigts hippocratiques. Dans trois cas le traitement de l'arthrite avait précédé de plusieurs mois le diagnostic de la lésion pulmonaire primordiale. L'ablation de la tumeur fit disparaître les symptômes articulaires sans faire rétrocéder les lésions périostiques.

Artritis Sintomática Debida a la Osteo-artropatia Pulmonar Hipertrófica en la Enfermedad Pulmonar Neoplásica

RESUMEN

Se comunica el caso de siete enfermos en los cuales osteo-artropatia estaba asociada a la neoplasia pulmonar. En cinco de ellos los dolores articulares parecían haber precedido los dedos hipocráticos. En tres casos el tratamiento de la artritis había precedido de varios meses el diagnóstico de la lesión pulmonar fundamental. La ablación quirúrgica del tumor hizo desaparecer los síntomas articulares sin hacer regresar las lesiones del periostio.